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[Translation done.]

CLAIM + DETAILED DESCRIPTION

[Claim(s)]
[Claim 1] The probe which is a probe used for measurement of the glutathione-S-transferase which participates in the glutathione conjugation in Homo sapiens, and is characterized by being chosen out of the oligonucleotide hybridized to each of each field of following the (1) - (17). (1) The field of 293-318 of GSTP1 gene (2) The field of 436-461 of GSTT1 gene (3) The field of 82-107 of GSTT2 gene (4) The field of 310-340 of a GSTM1B gene (5) The field of 310-338 of GSTM2 gene (6) The field of 323-353 of GSTM3 gene (7) The field of 322-354 of GSTM4 gene (8) The field of 342-310 of GSTM5 gene (9) The field of 316-347 of field (11) GSTA3 gene of 333-361 of field (10)

[Translation done.]

GSTA2 gene of 331-361 of one to GSTA1 gene (the position of registration number AF020919 of gene bank (GenBank) and the position from a start codon are unidentified)
(12) The field of 202-231 of field (13) MGST1 gene of 246-274 of GSTA4 gene (the position in the registration number U46498 of gene bank (GenBank) and the position from a start codon are unidentified)
(14) The field of 50-75 of field (17) GSTZ1 gene of 284-256 of field (16) MGST1L1 gene of 154-179 of field (15) MGST3 gene of 42-68 of MGST2 gene [Claim 2] The probe according to claim 1 which the reporter pigment and the quencher pigment have combined.
[Claim 3] The probe according to claim 1 whose length of a base sequence is 20-40.
[Claim 4] The probe according to claim 1 to 3 which is the thing including either of the arrangement shown in the arrangement number 1 - the arrangement number 17.
[Claim 5] The probe according to claim 1 to 3 which is either of the arrangement shown in the arrangement number 1 - the arrangement number 17.
[Claim 6] The primer pair of the forward primer and reverse primer which consist of an oligonucleotide which hybridizes the glutathione-S-transferase which participates in the glutathione conjugation in the Homo sapiens of following the (1) - (17) to following each field of the gene which carries out a code, respectively, And the measurement kit of glutathione-S-transferase chosen from the combination of the probe which consists of an oligonucleotide hybridized to the following field inserted into both the above-mentioned primers.
Primer pair; (1) 265 to 285 field and 342 -320 field of GSTP1 gene, probe; -- 293-318 field (2) primer pair; -- 414-434 field of GSTT1 gene -- and 500 to 478 field probe; -- 436-461 field (3) primer pair; -- 62-80 field of GSTT2 gene -- and 128 to 110 field probe; -- 82-107 field (4) primer pair; -- 217-237 field of a GSTM1B gene -- and 505 to 484 field probe; -- 310-340 field (5) primer pair; -- 220-240 field of GSTM2 gene -- and 434 to 413 field probe; -- 310-338 field (6) primer pair; -- 298-320 field of GSTM3 gene -- and 404 to 382 field probe; -- 323-353 field (7) primer pair; -- 298-318 field of GSTM4 gene -- and 431 to 410 field probe; -- 322-354 field (8) primer pair; -- 151-170 field of 170-190

field [of GSTM5 gene] and 388 -367 field, and probe;342-310 field (9) primer pair;GSTA1-1 gene, and 519 -501 field, probe; -- 331-361 field (10) primer pair; -- 199-220 field of GSTA2 gene -- and 522 to 500 field probe; -- 333-361 field (11) primer pair; -- 290-311 field of GSTA3 gene and 585 -561 field, and probe;316 -347 field (the position of registration number AF020919 of gene bank (GenBank) and the position from a start codon are unidentified)
Primer pair; (12) 191 to 211 field and 314 -293 field of GSTA4 gene, probe; -- 246-274 field (13) primer pair; -- 175-195 field of MGST1 gene and 255 -234 field, and probe;202 -231 field (the position in the registration number U46498 of gene bank (GenBank) and the position from a start codon are unidentified)
Primer pair; (14) 19 to 40 field and 162 -141 field of MGST2 gene, probe; -- 42-68 field (15) primer pair; -- 130-150 field of MGST3 gene -- and 200 to 180 field probe; -- 154-179 field (16) primer pair; -- 28-48 field of 218-238 field [of MGST1L1 gene] and 307 -289 field, and probe;284-256 field (17) primer pair;GSTZ1 gene and 161 -140 field, and probe;50 -75 field [Claim 7] The measurement kit according to claim 6 with which a probe combines a reporter pigment and a quencher pigment further.
[Claim 8] The measurement kit according to claim 7 chosen from the combination of the primer pair and probe which consist of an oligonucleotide including the arrangement shown by each arrangement number of the set shown in following the (1) - (17).
Primer pair; (1) The arrangement number 18 And 19, a probe; The arrangement number 1 Primer pair; (2) The arrangement number 20 And 21, a probe; The arrangement number 2 Primer pair; (3) The arrangement number 22 And 23, a probe; The arrangement number 3 Primer pair; (4) The arrangement number 24 And 25, a probe; The arrangement number 4 Primer pair; (5) The arrangement number 26 And 27, a probe; The arrangement number 5 Primer pair; (6) The arrangement number 28 And 29, a probe; The arrangement number 6 Primer pair; (7) The arrangement number 30 And 31, a probe; The arrangement number 7 Primer pair; (8) The arrangement number 32 And 33, a probe; The arrangement number 8 Primer pair; (9) The arrangement number 34 And 35, a probe; The arrangement number 9 Primer pair; (10)

The arrangement number 36 And 37, the probe; arrangement number 10 (11) primer pair; arrangement numbers 38 and 39, the probe; arrangement number 11 (12) primer pair; arrangement numbers 40 and 41, a probe; arrangement number 12 (13) primer pair; The arrangement number 42 And 43, the probe; arrangement number 13 (14) primer pair; arrangement numbers 44 and 45, the probe; arrangement number 14 (15) primer pair; arrangement numbers 46 and 47, a probe; arrangement number 15 (16) primer pair; arrangement numbers 48 and 49, probe; -- arrangement number 16 (17) primer pair; -- the arrangement numbers 50 and 51 and the probe; arrangement number 17

[Claim 9] It is a measurement kit according to claim 8, the set of (1) [the object for measurement of GSTP1] In the set of (2), the set of (3) by the object for measurement of GSTT1 [the object for measurement of GSTT2] In the set of (4), the set of (5) by the object for measurement of GSTM1B [the object for measurement of GSTM2] In the set of (6), the set of (7) by the object for measurement of GSTM3 [the object for measurement of GSTM4] In the set of (8), the set of (9) by the object for measurement of GSTM5 [the object for measurement of GSTA1-1] In the set of (10), the set of (11) by the object for measurement of GSTA2 [the object for measurement of GSTA3] In the set of (12), the set of (13) by the object for measurement of GSTA4 [the object for measurement of MGST1] the set of (14) -- the measurement kit whose set of (17) the set of (16) is [in the object for measurement of MGST2] an object for measurement of GSTZ1 in the object for measurement of MGST1L1 at the object for measurement of MGST3 in the set of (15).

[Claim 10] (1) according to claim 8 Measurement kit according to claim 9 chosen from the combination of the primer pair and probe which consist of an oligonucleotide which has the arrangement shown by each arrangement number of the set shown in - (17).

[Claim 11] [specimen / containing the glutathione-S-transferase which participates in the glutathione conjugation in Homo sapiens] The measuring method of glutathione-S-transferase characterized by performing polymerase chain reaction (PCR) using a measurement kit according to claim 6 to 10, and measuring the existence of hydrolysis of the used probe.

[Claim 12] The measuring method according to claim 11 with which the existence of hydrolysis is made by the existence of coloring of the fluorescence by excitation light radiation.

[Detailed Description of the Invention]
[0001]
[Field of the Invention] the [in / in this invention / Homo sapiens] -- it is related with the probe and kit the measuring method of the glutathione-S-transferase which participates in the glutathione conjugation which is a kind of II phase reaction, and for it.
[0002]
[Description of the Prior Art] the -- various things are known by the enzyme which participates in II phase reaction. Among these, the glutathione-S-transferase (glutathione S-transferase) shown below is enzyme which participates in glutathione conjugation.
(1) glutathione S-transferase pi (GSTP1) (2) glutathione S-transferase theta 1 (GSTT1) (3) Glutathione S-transferase theta 2 (GSTT2) (4) Glutathione S-transferase M 1B -- ((GSTM1B) 5) glutathione S-transferase M2 -- ((GSTM2) 6) glutathione S-transferase M3 -- ((GSTM3) 7) glutathione S-transferase M4 ((GSTM4)8) glutathione S-transferase M5 -- ((GSTM5) 9) glutathione S-transferase A1-1 -- ((GSTA1-1) 10) glutathione S-transferase A2 -- ((GSTA2) 11) glutathione S-transferase A3 -- ((GSTA3) 12) glutathione S-transferase A4 (GSTA4)(13) microsomal glutathione S-transferase -- ((MGST1) 14) microsomal glutathione S-transferase 2 -- ((MGST2) 15) microsomal glutathione S-transferase 3 (MGST3)(16) prostaglandin E synyhase (MGST1L1)(17) glutathione S-transferase Zeta 1 (GSTZ1)
[0003] the [by the way, / at the time of prescribing this new drug for the patient, when developing a new drug] -- it is important to grasp the motion (change in the amount of manifestations) of enzyme which participates in II phase reaction. the [because,] -- it is because the change in the effect of the concomitant drug agent used together with this new drug or side effects or the change in the effect of a new drug or side effects by a concomitant drug agent or other intake material cannot be predicted and the safety of this new drug cannot be checked, unless change of the enzyme

which participates in II phase reaction is known.
[0004] the [then, / in / on fields, such as the above-mentioned new drug development, and / Homo sapiens] -- development of the information about the enzyme which participates in II phase reaction, and the measurement technology which can distinguish and measure each molecular species, such as this, especially is demanded. If this technology can be developed, for example, an interaction with an agent besides a new drug, the influence of [at the time of special symptoms], etc. can grasp easily, the useful information about the side effects of this new drug can be acquired, and the safety of a new drug can be secured. On the other hand, polymerase chain reaction (PCR) is widely known as a method of amplifying nucleic acid, for example, RT-PCR (Reverse Transcription-PCR), competition tee TIBU RT-PCR, etc. demonstrate power in detection of a little mRNA(s), and a quantum.
[0005] The real-time quantum detecting method for having used PCR was established in recent years (Taq Man PCR (Genome Res., 6 (10))). 986 (1996) ABI PRISMTM Sequence Detection System (Applied Biosystems). This is the procedure of measuring nucleic acid using a specific fluorescent-labeling probe (TaqMan prove). It is in the status that Target DNA was made to anneal in more detail the probe which added and carried out fluorescent labeling of the quencher pigment, for example to the five prime end at the reporter pigment and the three-dash terminal, If the usual PCR reaction is made to perform, the above-mentioned probe will be hydrolyzed from a five prime end with advance of an extension reaction by the 5'-3' exonuclease activity which a DNA polymerase has. As a result, the reporter pigment of a five prime end separates from the quencher pigment of a three-dash terminal, and it is this, The FRET (Fluoresence Resonance Energy Transfer, fall phenomenon of fluorescence intensity based on the fall of energy ranking of reporter pigment by resonance of both fluorochromes) effect by having maintained a fixed spatial distance at the beginning is lost. The fluorescence intensity of the reporter pigment currently controlled by the quencher pigment increases. Therefore, target nucleic acid is alternatively detectable in fixed quantity on real time by measuring the increase in this fluorescence intensity. According to this procedure, agarose gel electrophoresis of

the amplification thing is carried out after a PCR reaction, for example, the complicated process of analyzing a migration pattern becomes unnecessary, and there is an advantage which is a short time and can do a fixed quantity of various samples simultaneously.

[0006] Since it is generally necessary to inspect to within a time [which was restricted very much about many specimens] to conduct a clinical test in the clinical test center etc., development of the procedure of the ability to inspect efficiently is demanded. The above-mentioned real-time detecting method is expected as a thing corresponding to such a request.

[0007] this invention persons pay their attention to the real-time detecting method by Above PCR -- this -- the [Homo sapiens] -- research was wholeheartedly repeated from II phase reaction, especially the idea whether it can use for detection of the glutathione-S-transferase which participates in glutathione conjugation.

[0008] However, glutathione-S-transferase which participates in the glutathione conjugation in the Homo sapiens who metabolizes the chemical substance known now, This etc. is made into a target gene, although it also amounts to about 17 sorts and the arrangement of each mRNA is known as mentioned above. It does not have the arrangement portion which overlaps mutually, but, moreover, could fully amplify on the same PCR conditions, and it was thought that the search of the oligonucleotide as each primer pair which can be hybridized in the specific position of this target gene itself was still more difficult. Moreover, it could hybridize under the same PCR condition earlier than primers, such as this, and construction of a specific probe was considered to be difficult the same way to the glutathione-S-transferase in Homo sapiens by the specific field inserted into this primer pair.

[0009] Especially the ease of carrying out of hybridization of two nucleic acid of known [nucleotide sequence], [the combination of the primer and probe which were chosen by this presumption of what can be presumed to some extent by calculation of a melting point (Tm)] [know / necessarily not bringing about a good result in DNA measurement] About the glutathione-S-transferase in all the Homo sapiens known now, this etc. was distinguished simultaneously and it was expected that the great experiment by an expert's trial

and error etc. was needed for selection of the combination of the each measurable primer pair for real-time detection and measurable probe by Above PCR.

[0010]

[Problem(s) to be Solved by the Invention] The purpose of this invention is to offer establishment and the probe of a sake of the measuring method by PCR of glutathione-S-transferase which participates in the glutathione conjugation in Homo sapiens, especially the real-time detecting method, and a primer pair.

[0011] As a result of repeating a great experiment and research and performing them about the glutathione-S-transferase which participates in glutathione conjugation from the above-mentioned purpose, this invention persons succeed in offering a primer pair receiving the enzyme concerned and the combination of a probe, and came to complete this invention of the following summary here.

[0012]

[Means for Solving the Problem] According to this invention, it is the probe used for measurement of the glutathione-S-transferase which participates in the glutathione conjugation in Homo sapiens. The following (1) - This probe that probe;, especially the reporter pigment which are characterized by being chosen out of the oligonucleotide hybridized to each of each field of (17), and the quencher pigment have combined; This probe; whose length of a base sequence is 20-40 This probe that is either of the arrangement shown in this probe; and the arrangement number 1 - the arrangement number 17 including either of the arrangement shown in the arrangement number 1 - the arrangement number 17 is offered.

(1) The field of 293-318 of GSTP1 gene (2) The field of 436-461 of GSTT1 gene (3) The field of 82-107 of GSTT2 gene (4) The field of 310-340 of a GSTM1B gene (5) The field of 310-338 of GSTM2 gene (6) The field of 323-353 of GSTM3 gene (7) The field of 322-354 of GSTM4 gene (8) The field of 342-310 of GSTM5 gene (9) The field of 316-347 of field (11) GSTA3 gene of 333-361 of field (10) GSTA2 gene of 331-361 of one to GSTA1 gene (the position of registration number AF020919 of gene bank (GenBank) and the position from a start codon are unidentified)

(12) The field of 202-231 of field (13) MGST1 gene of 246-274 of GSTA4 gene (the position in the registration number U46498 of gene bank (GenBank) and the position from a start codon are unidentified)
(14) The field of 50-75 of field (17) GSTZ1 gene of 284-256 of field (16) MGST1L1 gene of 154-179 of field (15) MGST3 gene of 42-68 of MGST2 gene [0013] Moreover, the primer pair of the forward primer and reverse primer which consist of an oligonucleotide which hybridizes the glutathione-S-transferase which participates in the glutathione conjugation in Homo sapiens to following each field of the gene which carries out a code, respectively according to this invention, And are chosen out of the combination of the probe which consists of an oligonucleotide hybridized to the following field inserted into both the above-mentioned primers. The measurement kit of the glutathione-S-transferase which participates in the glutathione conjugation in the Homo sapiens of following the (1) - (17); the above-mentioned measurement kit with which especially a probe combines a reporter pigment and a quencher pigment further is offered.
Primer pair; (1) 265 to 285 field and 342 -320 field of GSTP1 gene, probe; -- 293-318 field (2) primer pair; -- 414-434 field of GSTT1 gene -- and 500 to 478 field probe; -- 436-461 field (3) primer pair; -- 62-80 field of GSTT2 gene -- and 128 to 110 field probe; -- 82-107 field (4) primer pair; -- 217-237 field of a GSTM1B gene -- and 505 to 484 field probe; -- 310-340 field (5) primer pair; -- 220-240 field of GSTM2 gene -- and 434 to 413 field probe; -- 310-338 field (6) primer pair; -- 298-320 field of GSTM3 gene -- and 404 to 382 field probe; -- 323-353 field (7) primer pair; -- 298-318 field of GSTM4 gene -- and 431 to 410 field probe; -- 322-354 field (8) primer pair; -- 151-170 field of 170-190 field [of GSTM5 gene] and 388 -367 field, and probe;342-310 field (9) primer pair;GSTA1-1 gene, and 519 -501 field, probe; -- 331-361 field (10) primer pair; -- 199-220 field of GSTA2 gene -- and 522 to 500 field probe; -- 333-361 field (11) primer pair; -- 290-311 field of GSTA3 gene and 585 -561 field, and probe;316 -347 field (the position of registration number AF020919 of gene bank (GenBank) and the position from a start codon are unidentified)
Primer pair; (12) 191 to 211 field and 314 -293 field of GSTA4 gene, probe; -- 246-274 field (13) primer pair; --

175-195 field of MGST1 gene and 255 -234 field, and probe;202 -231 field (the position in the registration number U46498 of gene bank (GenBank) and the position from a start codon are unidentified)
Primer pair; (14) 19 to 40 field and 162 -141 field of MGST2 gene, probe; -- 42-68 field (15) primer pair; -- 130-150 field of MGST3 gene -- and 200 to 180 field probe; -- 154-179 field (16) primer pair; -- 28-48 field of 218-238 field [of MGST1L1 gene] and 307 -289 field, and probe;284-256 field (17) primer pair;GSTZ1 gene and 161 -140 field, and probe;50 -75 field [0014] The thing including the arrangement shown by each arrangement number chosen from following the (1) - (8) as what has a desirable combination (set) of the primer pair and probe which constitute the above-mentioned kit, and the thing of the arrangement more preferably shown by each arrangement number can be mentioned.
Primer pair; (1) The arrangement number 18 And 19, a probe; The arrangement number 1 Primer pair; (2) The arrangement number 20 And 21, a probe; The arrangement number 2 Primer pair; (3) The arrangement number 22 And 23, a probe; The arrangement number 3 Primer pair; (4) The arrangement number 24 And 25, a probe; The arrangement number 4 Primer pair; (5) The arrangement number 26 And 27, a probe; The arrangement number 5 Primer pair; (6) The arrangement number 28 And 29, a probe; The arrangement number 6 Primer pair; (7) The arrangement number 30 And 31, a probe; The arrangement number 7 Primer pair; (8) The arrangement number 32 And 33, a probe; The arrangement number 8 Primer pair; (9) The arrangement number 34 And 35, a probe; The arrangement number 9 Primer pair; (10) The arrangement number 36 And 37, the probe; arrangement number 10 (11) primer pair; arrangement numbers 38 and 39, the probe; arrangement number 11 (12) primer pair; arrangement numbers 40 and 41, a probe; arrangement number 12 (13) primer pair; The arrangement number 42 And 43, the probe; arrangement number 13 (14) primer pair; arrangement numbers 44 and 45, the probe; arrangement number 14 (15) primer pair; arrangement numbers 46 and 47, a probe; arrangement number 15 (16) primer pair; arrangement numbers 48 and 49, probe; -- arrangement number 16 (17) primer pair; -- the arrangement numbers 50 and 51 and the probe; arrangement number 17

[0015] Moreover, each above-mentioned set can be an object for measurement of the following enzyme, respectively.